the negative sodium balance.[9] As Dr. Mendoza indicates, hypertonic saline, therefore, is not the treatment of choice in SIADH but rather a negative water balance is the goal. In chronic cases of SIADH water restriction is the preferred method of treatment. Recently, it has been shown that even with acute, symptomatic hyponatremia, hypertonic saline need not be used. The therapeutic approach described is to rapidly increase free-water clearance and correct hyponatremia by inducing diuresis with furosemide, as the urinary electrolyte losses are concomitantly replaced by a parenteral hypertonic infusion.[10] Such an approach avoids further volume expansion in patients with SIADH who already have an excess volume of total body fluids. Moreover, as Dr. Mendoza emphasizes, in the presence of this volume expansion the hypertonic saline load will be rapidly excreted.[6]

Since volume status, and not serum sodium concentration, is the main determinant of urinary sodium concentration and excretion, the authors' statement, "when the serum sodium concentration is low, it is appropriate to have a urine sodium concentration of nearly zero, with subsequent sodium retention and correction of the hyponatremia," is misleading. Urinary sodium concentration in patients with SIADH, as in normal subjects, can reach zero to 1 mEq per liter when their intake of sodium is restricted.[9] The high urinary sodium concentration in patients with SIADH is primarily related to the fact that their sodium intake must be excreted in a small volume of urine and thus necessitates a high urine sodium concentration. It is therefore important to re-emphasize that the primary defect in SIADH is that of water retention and thus, until inhibitors of ADH are available, a negative water balance achieved either by water restriction or diuretic-induced free-water losses would seem to be the most "appropriate" means of treatment. Since the role of a negative sodium balance in the pathogenesis of the hyponatremia of SIADH is negligible, the use of hypertonic saline in the treatment would seem "inappropriate."

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The Impact of Recent Findings Concerning Vitamin D Metabolism on Clinical Medicine

PERHAPS ONE OF THE most important medical advances in the last decade is the discovery that vitamin D must be converted to a hormone or hormones before it can carry out its known functions. The only known hormone produced from vitamin D is 1,25-dihydroxyvitamin D_3 ($1,25[OH]_2D_3$) but others may follow in view of the multiple activities of vitamin D. Of great importance is the fact that $1,25(OH)_2D_3$ production is feedback regulated by both serum calcium and serum phosphorus concentrations either directly or indirectly. The serum calcium regulation is mediated by the parathyroid glands with the parathyroid hormone stimulating synthesis of $1,25(OH)_2D_3$. The actual cellular or molecular mechanism of the regulation is not understood at the present time but at least it is important to realize that serum calcium and serum phosphorus feedback controls the synthesis of a hormone ($1,25[OH]_2D_3$) whose responsibility is to elevate the concentration of these ions in the plasma. Additionally, it must be recognized that regulation of the 25-hydroxyvitamin D_3-1-hydroxylase does not take place in vitamin D deficiency.

The article by Coburn and his associates discusses the regulation of $1,25(OH)_2D_3$ production but the picture presented is not clear and it is uncertain whether these authors believe that parathyroid hormone is an important regulator, a concept firmly held by a number of investigators in the field. This is particularly an important concept in

view of the fact that 1 μg per day of $1,25(OH)_2D_3$ (50 units by Coburn et al definition) is effective in maintaining serum calcium of hypoparathyroid patients in the normal range provided dietary calcium is adequate.

The molecular and cellular mechanisms whereby $1,25(OH)_2D_3$ elevates calcium and phosphorus in the plasma by increasing intestinal calcium transport or bone mobilization are far from understood. Wasserman and his colleagues have made an important contribution to this area in demonstrating the existence of calcium binding protein in intestine which appears in response to vitamin D. Beyond that, little is established and it is of some concern that the action of $1,25(OH)_2D_3$ is assumed to be like that of such steroid hormones as estrogen, aldosterone and testosterone. Although this may prove to be the case, it is prejudicial to assume it. Chemically vitamin D may be classified as a steroid only because it is derived from a precursor which possesses a steroid nucleus. However, structurally the resemblance of $1,25(OH)_2D_3$ to a steroid is vague at best. Whether some or all of the actions of $1,25(OH)_2D_3$ are mediated by nuclear interaction is also not known. It is, therefore, essential to keep an open mind regarding the mechanism of $1,25(OH)_2D_3$ action until clearly definitive results are obtained.

The potential clinical importance of $1,25(OH)_2D_3$ and 25-OH-D_3 and their analogs is indeed obvious in such diseases as renal osteodystrophy, vitamin D dependency disease, hypoparathyroidism and Dilantin®*-phenobarbital induced bone disease. Furthermore, other bone diseases and disturbances of calcium metabolism may be related to disturbances in vitamin D metabolism or at least may be benefited by treatment with vitamin D metabolites. In the article by Coburn et al attention is paid to a number of these diseases and their potential relationship to vitamin D metabolism. These considerations are important, suggestive and very much worthy of thoughtful consideration. In addition, the article represents an attempt to provide information on vitamin D metabolism to the clinician. Although very useful, there is a Southern California bias to the article with omissions of some papers which bear on such important matters as biological activity of $1,25(OH)_2D_3$ and its analogs. However, all review articles have in them blind spots, prejudices and omissions and the readers are urged to examine a variety of reviews by various authors to gain a balanced perspective of this potentially important clinical area.

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*diphenylhydantoin.

Top Flight Brains for Medicine

A CAREER IN MEDICINE appears to be the goal of an unprecedented number of college students. Exact figures are difficult to come by, partly because career goals for many students often change before, during and after college, and partly because most colleges and universities have no accurate means of determining who is a committed premedical student and who is not. But an informal survey of some of the leading universities in the West indicates they believe that as many as ten percent of their college undergraduates are pointed toward careers in medicine. This is an awesome number, and an awesome responsibility for the colleges and universities to try to provide the amount and kind of instruction this number of students expect and believe they need. And it is dismaying to realize that only a small proportion of these students, even the highly dedicated and determined, will ever achieve their goal of becoming physicians.

For medicine, it means that medical schools will have several fully qualified applicants for each position in the first-year class and the likelihood is that those who are accepted will be more than fully qualified. They will have top flight brains, as well as dedication and determination. All this is happening at a time when many physicians in practice take a dim view of the future of medicine and what they foresee as the result of increasing government intervention in medicine and patient care. The new generation apparently does not see this as a deterrent. Rather it seems likely that their intelligence, vigor, independence and determination will turn out to be more than a match for any clumsy and sluggish governmental bureaucracy with which it is likely they will have to deal.

Thus it appears that medicine will have more than its fair share of top flight brains for the foreseeable future, and this surely augurs well for patient care and for the practice of medicine.

—MSMW